UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,507	05/15/2006	Per Sonne Holm	BOH06278P00200US	7523

32116 7590 10/28/2008

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
500 W. MADISON STREET
SUITE 3800
CHICAGO, IL 60661

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
10/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,507	HOLM, PER SONNE	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *1-29 and 36-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 May 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-70 are pending in this application.

Election/Restrictions

Applicant's election without traverse of E1b in the reply to the species requirement filed on 7/22/08 is acknowledged. Claims 1-29 and 36-70 had not been subjected to restriction requirement, as the meanings of the claims are so unclear. First, claims 1-29 and 36-69 are directed to "use of' products, which is not a recognized class of inventions under 35 USC 101. As well claim 70 as well as claims 4, 7, 8, 10, 11, 14, 15, 17, 19, 20, 22-24, 27, 36, 38, 40-44, 46-52, 54, 56, 59-62, 64, 65, 67 and 68 are improper multiple dependent claims that do not refer to the claims in the alternative. As well, they depend from another multiple dependent claim, e.g. claim 68. See MPEP § 608.01(n). The claims have not been amended and remain withdrawn. Election was made **without** traverse in the reply filed on 7/22/08.

Information Disclosure Statement

An IDS filed 1/31/08 has been identified and the documents considered. The signed and initialed PTO Form 1449 has been mailed with this action.

Specification

The title of the invention, *Novel use of Adenoviruses and nucleic acid that code for said viruses*, is not descriptive. A new title is required that is clearly indicative of the invention to

which the claims are directed. The use of novel in the title is objected to as inventions before the US Patent and Trademark Office are presumed to be novel.

The disclosure is objected to because of the following informalities: --Brief Description of the Drawings-- should be inserted prior to the description of Figure 1 on page 53. MPEP 608.01(a). Appropriate correction is required.

Drawings

Figure 14 is objected to under 37 CFR 1.83(a) because they fail to show any details as described in the specification. Specifically, figure 14 is a photograph of a mouse. However, the details are indiscernible as the image is too dark. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, figure 24 contains a sequence that is not identified by sequence identifier numbers.

If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:. If not, a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, CRF and letter stating that the contents of the sequence listing and the CRF are the same and contain no new matter is required. **The nature of the non-compliance did not preclude the examination on the merits of the instant application, the results of which follow.**

Claim Objections

Claims are 30-35 are objected to because of the following informalities: Each of the claims requires an article. It is noted that the Independent claim should begin with the article "A" or "An" and subsequent claims dependent from this claim should refer to that claim using "The claim".

As well in claim 30, the descriptions of the functions of the viral oncogene are grammatically incorrect and require a verb. For example, in (a), "transactivation" can be amended to --mediates transactivation-- and in step (b) --does not induce YB-1 activity--. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30-35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to recite "isolated" or "purified". Specifically, the recitation of a viral oncogene protein does not distinguish from an oncogene that is in nature. The recitation that it is preferably isolated is non-limiting. As well, natural mutant or deleted variants of native viral oncogenes are found in nature. The claims do not distinguish between these and isolated proteins.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-35 refer to mutations in "the CR3 region" The N-terminus" and "the C-terminus". However as concerns claim 30, these claims lack antecedent basis. Also recitation of "the wild-type" lacks antecedent basis.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a viral oncogene protein such as E1A that mediates transactivation of at least on viral gene such as E1B-55K and also does not induce activity YB-1 in a nucleus of a cell in which the oncogene is present. As well, the viral oncogene in claims 32 and 34 can have one or several mutations or deletions compared to "the wildtype oncogene protein". The mutations are not structural limited to specific mutations. Whereas the deletions must be selected from the group consisting of "the CR3 region", the M-terminus" and "the C-terminus", neither the mutations nor the deletions are limited in size. Hence, the claims encompass an enormous number of mutations of an enormous number of oncogenes. The scope of the invention is extremely broad. The claims have been limited through a species requirement to E1A which does not ameliorate the large number of mutants that are encompassed by the claims.

The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice,

reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

Applicants characterize the effect of mutations in E1A with the goal of a designing a protein that activates E1B but does not activate YB-1.

As well, mutants that bind RB or cannot are claimed. The specification teaches,

> In order to confer the capability to not bind to Rb, the following deletions of the E1A oncoprotein are, for example, possible: Deletion in the CR1 region (amino acid positions 30-85 in Ad5) and deletion of the CR2 region (amino acid positions 120-139 in AD5). In doing so, the CR3 region is maintained and can have its transactivating function on the other early viral genes.
>
> In contrast thereto, the following deletions to the E1A oncoprotein are in principle possible in order to impart E1A the capability to bind to Rb: deletion of the CR3 region (amino acid positions 140-185); deletion of the N-terminus (amino acid positions 1-29); deletion of amino acid positions 85-119; and deletion of the C-terminus (amino acid positions 186-289). The regions recited herein do not interfere with the binding of E2F to Rb. The transactivating function remains, however, is reduced compared to wildtype Ad5.

As regards the mutations in E1A, The specification does not provide any information on what amino acid residues in particular are necessary and sufficient for the combined function of lack of transactivation of YB-1, transactivation of E1B55k and loss of or maintenance of Rb binding. The specification also provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in E1A polypeptide that would improve or at least would not interfere with the biological activity or

structural features necessary for the biological activity and stability of the protein. It is not possible to even guess at the amino acid residues which are critical to its structure or function based on sequence conservation. Furthermore, it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see below). As regards deletions in the CR3 region, N-terminus, C-terminus, CR1 and/or Cr2, applicants only disclose one deletion in the CR1 region (amino acid positions 30-85) and one in the CR2 region (120-139 of Ad5) that lead to loss of RB binding. Deletions that do not affect Rb binding the specification teaches one deletion in the CR3 region of amino acids 140-185 one in the N-terminus 1-29 a deletion in 85-119 and one deletion in the C-terminus 186-129. All of these mutations are in the E1A region of Ad5. The scope of these deletions is not commensurate in scope with the broad genus of any oncogene that transactivates E1b-55K but does not activate YB-1 further comprising one or several mutations or deletions.

An adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of claimed nucleic acid sequences. A particular protein sequence determines the protein's structural, and functional properties, and the ability to determine a priori whether a homologue or variant can function in the recited invention is not a high art. A knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant

to modification), and detailed knowledge of the ways in which a protein's structure relates to its functional usefulness is required (see Guo et al and Lesk et al). By claiming all viral oncogenes with the functional properties described in terms of transactivation ability and binding without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See Fiers 7. Reveb 25 USPQZd 1601 (CA FC 1993) and Regents of the Univ. Calif v. Eli Lilly & Co. 43 USPQZd 1398 (CA FC, 1997)). In this case, applicants have only disclosed Ad5 E1A deletions in which the resulting protein can mediate E1B transactivation but not YB-1 and can or cannot bind Rb. Given the large size and diversity of fragments generated by mutation or deletion CR1, CR2, CR3 or at the N and/or C-terminus and the inability to determine which will also have the essential element, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of no species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-35 are rejected under 35 U.S.C. 102(b) as being rejected by LaFace et al (US 6,649,158; see entire document).

LaFace teaches mutations in E1a that will and will not affect Rb binding. "In the preferred practice of the invention, the Rb binding deletions are represented by elimination of amino acids from about 111-127, preferably from about 111-123. More preferred is a vector wherein said deletion in the E1a-p300 binding domain comprises a deletion of the codons for amino acids 4 to 25 of the adenoviral E1a gene product. More preferred is a vector wherein deletion in the E1a-Rb binding domain comprises a deletion of the codons for amino acids 111-123 of the adenoviral E1a gene product". Absent evidence to the contrary such an oncogene will given the similarity to the instant deletions mediate transactivation of E1B-55K and not for YB-1 binding.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich, PhD/
Primary Examiner, Art Unit 1633